

HISTOLOGICAL EXAMINATION OF THE EYES

FROM

A Case of Pernicious Anaemia.

BY G. E. DE SCHWEINITZ, M.D.

PHILADELPHIA, PENN.

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HISTOLOGICAL EXAMINATION OF THE EYES FROM A CASE OF PERNICIOUS ANÆMIA.

BY G. E. DE SCHWEINITZ, M.D.,

PHILADELPHIA, PENN.

The following case of pernicious anæmia occurred in the wards of the Philadelphia Hospital in the service of Dr. F. P. Henry, to whose courtesy I am indebted for the privilege of examining the eyes.

Dr. Charles W. Burr* has reported the case, so far as the lesions of the spinal cord are concerned, and from his paper I abstract the following history :

James Mullaney, male, 64 years of age, a laborer, was admitted to the Philadelphia Hospital, April 26, 1894. He had been slowly growing weaker for several years and complained of slight dyspnœa upon exertion. During his entire stay in the hospital his only complaint was a progressive weakness.

There was a soft systolic murmur at the apex and a more distinct systolic murmur at the aortic cartilage, transmitted to the vessels of the neck.

At the first examination of the blood made by Dr. Henry

* University Medical Magazine, April, 1895.

there were 1,275,000 red blood corpuscles to the cubic millimetre. At a later examination made by Dr. Daland, the hæmatokrit being used, there were 25 per cent. of the normal number of red blood corpuscles. Fleischl's hæmoglobinometer gave 20 per cent. of hæmoglobin.

The knee-jerks were abolished. The urine contained neither sugar nor albumin. Examination of the liver, lungs, spleen, and kidneys, failed to develop signs of disease. The skin was exceedingly pale, and there was a freckle-like pigmentation over the entire body, except on the palms and soles.

When I examined the eyes, two days before death, the usual ophthalmoscopic appearances of intense anæmia were present, namely, rather narrow arteries, broad, pale veins, intense pallor of the fundus, over portions of which, chiefly in the periphery, there was a faint, fog-like œdema, and hemorrhages somewhat flame-shaped, but also irregular and splotchy, only in the neighborhood of the papilla. A few of the hemorrhages contained a whitish center, and here and there throughout the eye-ground there were small white or yellowish-white spots. The optic discs, with the exception of being exceedingly pallid, were unchanged. The examination was made when the man was too weak to be raised in the sitting posture, and was necessarily less prolonged than was desirable.

The post-mortem examination was made twenty-four hours after death, and the findings were largely negative. There was only a small amount of intensely yellow subcutaneous fat; the tibial marrow was slightly tinged with red. The lesions of croupous pneumonia and an old endocarditis were visible.

The only tissues submitted to microscopic examination were the spinal cord and the eyes. As already stated, the spinal cord has been described by Dr. Burr, who found at the lowest level of the crossing pyramids degeneration of the posterior columns, but not extending to the border of the gray matter. In the lateral columns there was a small area of degeneration at the periphery, just outside of the posterior horns. In the cervical swelling there was a patchy degeneration affecting the whole transverse area of the posterior columns, and much more pronounced in some fields than others. In the lateral tracts

there was a wedge-shaped area of degeneration just external to the posterior horns. The same condition obtained in the dorsal region. The lumbar cord was not examined. The gray matter and the posterior peripheral roots were not affected.

The eyes were hardened in Müller's fluid, imbedded in paraffine, and cut in serial sections.* As the conditions were practically the same in each eye, a record of one will be sufficient.

The optic nerve entrance is slightly cupped, the nerve bundles viewed in longitudinal section have a yellowish tint, and there is some increase in the number of nuclei. Cross sections of the optic nerve stained by the Weigert-Pal method do not exhibit degenerative change or atrophy. An attempt to develop the Deiter cells by the Golgi-Cajal method gave negative results, probably owing to the fact that the preservation of the specimens had been in Müller's fluid, although Berkley's modification of Golgi's method, which is suited to Müller-fluid-hardened specimens, yielded equally negative results.

The cornea, iris, ciliary body, and choroid are normal, the lesions being confined entirely to the retinal elements.

Anterior to the equator of the eyeball there are no hemorrhages, but the retinal elements are somewhat indistinct and show a tendency to separate one from the other. As the ora serrata is approached, this tendency develops into the lesions of a marked œdema, the tissue between the inner nuclear layer and outer limiting membrane containing large oval empty spaces, so sharply marked in some instances as to present appearances analogous to the so-called cystic degeneration. This œdema apparently begins in the outer reticular layer and gradually involves the outer granule layer, until the tissue between the internal nuclear layer and the outer limiting membrane becomes occupied, if I may so express myself, with a series of oval cavities separated by thickened bundles of fibres in which may be seen imbedded the remains of the nuclei. (Figure I.)†

Posterior to the equator and in the neighborhood of the optic entrance are the hemorrhages, appearing as extravasations of

* I am indebted to Dr. J. Dutton Steele for the preparation of the sections.

† The drawings illustrating this paper were made by Mr. E. F. Faber of Philadelphia.

blood corpuscles disposed in various positions in the retinal layers. The chief extravasations are found in the nerve fibre layer and among the ganglion cells; hemorrhages also appear in the outer and inner reticular layers. For the most part the retinal vessels, especially the veins, are stuffed with corpuscles. In a few places, both veins and arteries are empty. (Figure II.)

In addition to the lesions thus far described, there are great thickening of the nerve fibre layer and varicose enlargement of the fibres. A typical diseased area of this character presents itself as a round or slightly oval mass which springs from the nerve fibre layer and pushes outward, pressing the overlying retinal layers until it almost obliterates the internal reticular layer, practically causing the internal and external granule layers to come in contact, inasmuch as they are separated only by a thin stratum of compressed external reticular tissue. In some places this lesion is capped with a layer of blood cells which occupies the position of the ganglion and internal granule layers. In others there is absence of hemorrhagic exudation. The center of a focus of pathological change of this character is composed of variously shaped but chiefly roundish and globular bodies of homogeneous structure. These bodies do not stain with the ordinary pigments used in microscopic work,—carmine and hæmatoxylin. Instead of large masses, smaller ones also exist, lying directly in the center of the nerve fibre layer, and crossed above and below with intact fibres. In some places the varicosities are more isolated, that is to say, there is no conglomerate collection; in fact, the bodies do not look unlike badly-stained ganglion cells, a comparison which has already been made by Uhthoff, to whose research I shall presently refer. (Figure III.)

In summary, I may say that the histological changes found in this case of pernicious anæmia were: (*a*) hemorrhages in the various strata of the retina, but most marked in the nerve fibre layer; (*b*) varicose hypertrophy of the fibres of the nerve fibre layer, existing either as an isolated lesion or sometimes gathered in a conglomerate mass; and (*c*) exquisite œdema of the retina, especially in its periphery, an œdema beginning in the outer reticular layer and gradually involving the outer granule layer,

until the space between the internal nuclear layer and the outer limiting membrane becomes riddled with a series of oval cavities.

These microscopic findings correspond closely with the ophthalmoscopic picture: (*a*) flame-shaped and irregular hemorrhages in the neighborhood of the papilla; (*b*) hemorrhagic areas containing a yellowish center, or isolated yellowish-white spots which probably correspond to the hypertrophied and degenerated nerve fibres which have been described; and (*c*) a cloud-like œdema, which was most marked in the retinal periphery.

Uththoff* in a description of the pathological retinal changes in progressive pernicious anæmia, based upon the examination of three cases, summarizes his findings in a very analogous manner, namely, hemorrhages in the various retinal layers, varicose hypertrophy of the non-medullated nerve fibres, and glistening colloid masses of varying size and shape in the internuclear layer.

Uththoff was unable to find collections of round cells in the center of the hemorrhages, as they have been described by Litten, nor did he detect in the midst of the hemorrhages collections of round colorless cells enclosed in capsules, which Manz† believed to be the wall of a capillary dilatation. Neither are these lesions present in my case. I was unable to find the glistening colloid bodies in the internuclear layer which Uththoff has described. These bodies, however, were present in only one of his cases. In Uththoff's sections the collections of diseased fibres were confined chiefly to the inner portion of the nerve fibre layer, and usually protruded into the vitreous; occasionally they were situated in the middle of the nerve stratum, and normal fibres crossed them above and below: rarely the thickening pressed outward and the overlying retinal layers were flattened. As already described, the last-named condition is the rule in my specimen; in no portion of the sections is there a protrusion of any of the masses into the vitreous.

Ophthalmoscopically, Quincke has observed œdema of the

* Klin. Monatsbl. f. Augenheilk., 1880, XVIII, page 513.

† Centralbl. f. die med. Wissenschaften, Berlin, 1875, page 675.



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Figure 1.

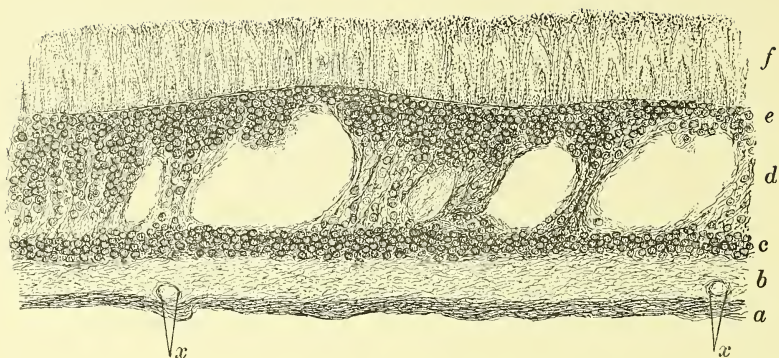
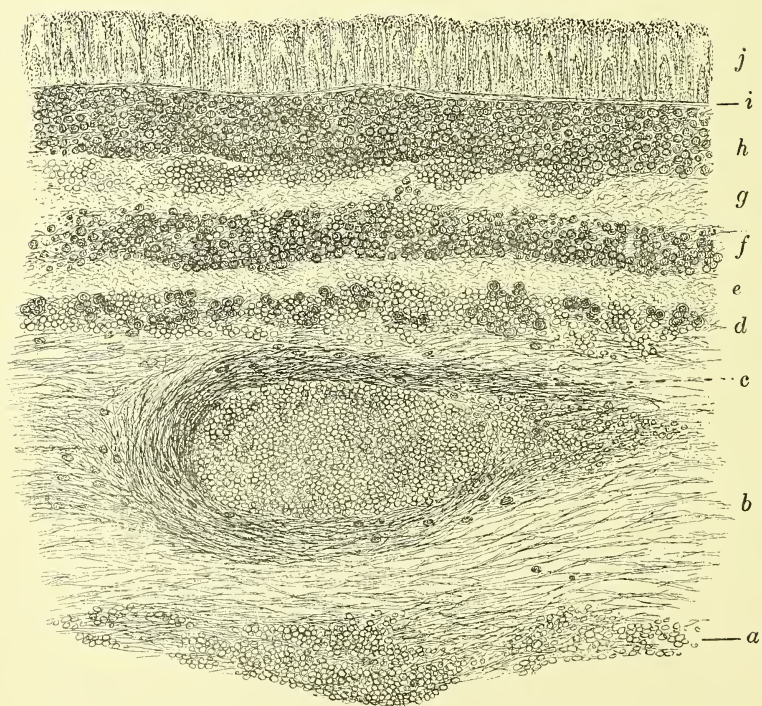


Figure II.



retina, just as I did, an œdema which is further demonstrable by the microscopic examination. Writing on profound affections of the eyes in pernicious anæmia, Dr. Elizabeth Sargeant,† in addition to extensive retinal hemorrhages and detachment, describes extensive œdema of the retina near the equator, while in the immediate neighborhood of the papilla the granular layers were stretched by the œdema into reticular tissue, cystic degeneration being present in the ora serrata. She ascribes the changes in the eyes to œdema and extravasation caused by the general lowered vitality of the vascular system, inflammatory symptoms being secondary and circumscribed.

Natanson† has had the opportunity of examining three cases of the so-called anæmia perniciosa helminthiatica, and found ophthalmoscopically and microscopically practically the same conditions which have been described in essential pernicious anæmia. He also observed a delicate œdema of the retina.

Uthhoff believes, on the ground of the pathologico-anatomical changes which he has found, that we are justified, as in leucæmia, in describing the retinal changes of pernicious anæmia as a true retinitis. At all events, to quote his sentence, pernicious anæmia appears to serve as the foundation for that essential process which has been described as varicose hypertrophy of the nerve fibres. Other than this condition, which was present also in my sections, inflammatory symptoms are entirely lacking. Inflammatory symptoms were not demonstrable in Natanson's cases, and this author believes that the retinal hemorrhages have a not unimportant diagnostic and prognostic significance as to the morphological changes in the blood, inasmuch as we may expect any patient suffering from micro- or poikilo-cytosis to have retinal hemorrhages and the reverse. Therefore, if these hemorrhages are found, morphological changes in the blood may be certainly inferred, even without microscopic examination of this fluid.

* Archives of Ophthalmology, XXI, 1892, page 39.

† Abstract in Nagel's Jahresbericht der Ophthalmologie, XXV, 1895, page 528.

DESCHWEINITZ: *Case of Pernicious Anæmia.*

EXPLANATION OF FIGURES.

Figure I.—Retina with Œdema. Pernicious Anæmia.

a, b, Fibre layer and inner reticular layer; *c*, compressed inner nuclear layer; *d*, tissue of the outer reticular and outer nuclear layer, confluent and containing large empty spaces; *e*, outer limiting membrane; *f*, rod and cones; *x*, blood vessels. (Zeiss. Compens-ocular, 4; obj. 4.0 mm., apert., 0.95.)

Figure II.—Retinal Hemorrhages. Pernicious Anæmia.

a, Hemorrhagic extravasation at inner portion of fibre layer bulging toward vitreous; *b*, thickened fibre layer, with large artery; *c*, distended with corpuscles; *d*, ganglion layer infiltrated with blood corpuscles; *e*, inner reticular layer, comparatively normal; *f*, inner nuclear layer, slightly involved in hemorrhagic process; *g*, outer reticular layer, markedly infiltrated with blood corpuscles which encroach on *h*, the outer nuclear layer; *i*, outer limiting membrane; *g*, rod and cones. (Ampl. ditto.)

Figure III.—Varicose Hypertrophy of the Nerve Fibres. Pernicious Anæmia.

a, Conglomerate mass of varicose nerve fibres, occupying entire width of fibre layer; *b*, hemorrhage capping thickened fibres lying partly in ganglion layer—inner reticular layer not distinguishable; *c*, inner nuclear layer somewhat compressed; *d*, outer reticular layer; *e*, outer nuclear layer; *f*, outer limiting membrane; *g*, rods and cones. (Ampl. ditto.)

DISCUSSION.

DR. E. KNAPP. My attention was attracted to the angiod streaks many years ago, and sometimes the picture is very peculiar. Here are the pictures of some cases that are interesting. I may point to a picture I saw many years ago which has until lately been mysterious to me, and which I think suffers no other explanation than this. I will draw it upon the blackboard (drawing). There is, I think, such a picture in Jaeger's Atlas. The background is normal, except that it is pervaded by long lines crossing the retinal vessels all over the fundus. They are nearly parallel or slightly curved. I am convinced that they are the result of hemorrhages. If we follow hemorrhages for years, we can find almost every change. After a hemorrhage I think the blood corpuscles lie more or less loose in the retina, and are by the tissue currents collected in lines or irregular figures, such as we see in the sand at the seashore. After hemorrhages all kinds of transient forms can be noticed, from the lines shown by Dr. de Schweinitz to the end stage, where, with a more or less normal fundus, we have before us a system of figures which at first appears utterly mysterious.

Figure III.

